=> fil hcapl; d que l24; d que l27; s l24 or l27; fil medl; d que l35; d que l42; d que l44; s l44 or l42 or l35
FILE 'HCAPLUS' ENTERED AT 12:40:46 ON 31 MAY 2001
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FILE COVERS 1947 - 31 May 2001 VOL 134 ISS 23
FILE LAST UPDATED: 30 May 2001 (20010530/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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L11	84	SEA FILE=HCAPLUS ABB=ON	GRO BETA OR GROBETA
L12	4437	SEA FILE=HCAPLUS ABB=ON	CHEMOKINE#/CW
L13	1336	SEA FILE=HCAPLUS ABB=ON	ANTI-INFECTIVE AGENTS/CT
L14	4280	SEA FILE=HCAPLUS ABB=ON	ANTIMICROBIAL AGENTS/CT
L15	14421	SEA FILE=HCAPLUS ABB=ON	ANTIBACTERIAL AGENTS/CT
L16	53883	SEA FILE=HCAPLUS ABB=ON	FUNGICIDE#/CW
L17	9389	SEA FILE=HCAPLUS ABB=ON	ANTIVIRAL AGENTS/CT
L18	15271	SEA FILE=HCAPLUS ABB=ON	"VIRUCIDES AND VIRUSTATS"/CT
L19	56802	SEA FILE=HCAPLUS ABB=ON	INFECTION+NT/CT
L20	14	SEA FILE=HCAPLUS ABB=ON	L11(L)THU/RL — Role - Therapeutic use
L21	13	SEA FILE=HCAPLUS ABB=ON	L12(L)THU/RL AND L11
L22	16	SEA FILE=HCAPLUS ABB=ON	L11 AND PHARMAC?/SC,SX
L24	9	SEA FILE=HCAPLUS ABB=ON	((L20 OR L21 OR L22)) AND ((L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19))

L11	84	SEA FILE=HCAPLUS ABB=ON	GRO BETA OR GROBETA
L12	4437	SEA FILE=HCAPLUS ABB=ON	CHEMOKINE#/CW
L20	14	SEA FILE=HCAPLUS ABB=ON	L11(L)THU/RL
L21	13	SEA FILE=HCAPLUS ABB=ON	L12(L)THU/RL AND L11
L22	16	SEA FILE=HCAPLUS ABB=ON	L11 AND PHARMAC?/SC,SX
L23	23	SEA FILE=HCAPLUS ABB=ON	((L20 OR L21 OR L22))
L25	4969	SEA FILE=HCAPLUS ABB=ON	GRANULOCYTE COLONY STIMULATING OR GCSF
L26	6083	SEA FILE=HCAPLUS ABB=ON	L25 OR G CSF
L27	4	SEA FILE=HCAPLUS ABB=ON	L23 AND L26

L74 11 L24 OR L27

Searched by Barb O'Bryen, STIC 308-4291

FILE 'MEDLINE' ENTERED AT 12:40:48 ON 31 MAY 2001

FILE LAST UPDATED: 29 MAY 2001 (20010529/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains new records from the former NLM HEALTH STAR database. These records have an Entry Date and Update Date of 20010223.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

subheading-

```
L29          43 SEA FILE=MEDLINE ABB=ON  GRO BETA OR GROBETA
L32      139603 SEA FILE=MEDLINE ABB=ON  C1.252./CT(L)TH./CT - Bacterial infections (l) therapy
L33       22611 SEA FILE=MEDLINE ABB=ON  MYCOSES+NT/CT(L)TH./CT - subheading-therapy
L34      107676 SEA FILE=MEDLINE ABB=ON  C2./CT(L)TH./CT = Virus diseases (l) subheading-therapy
L35           1 SEA FILE=MEDLINE ABB=ON  L29 AND ((L32 OR L33 OR L34))
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L29          43 SEA FILE=MEDLINE ABB=ON  GRO BETA OR GROBETA
L39       12104 SEA FILE=MEDLINE ABB=ON  ANTIFUNGAL AGENTS/CT
L40       18687 SEA FILE=MEDLINE ABB=ON  ANTIVIRAL AGENTS/CT
L41       15116 SEA FILE=MEDLINE ABB=ON  ANTI-INFECTIVE AGENTS/CT
L42           1 SEA FILE=MEDLINE ABB=ON  L29 AND ((L39 OR L40 OR L41))
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L29          43 SEA FILE=MEDLINE ABB=ON  GRO BETA OR GROBETA
L43       30572 SEA FILE=MEDLINE ABB=ON  COLONY-STIMULATING FACTORS+NT/CT
L44           2 SEA FILE=MEDLINE ABB=ON  L29 AND L43
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L75           3 L44 OR L42 OR L35
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=> fil embase; d que l49; d que l62; s l49 or l62
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FILE 'EMBASE' ENTERED AT 12:41:08 ON 31 MAY 2001

FILE COVERS 1974 TO 23 May 2001 (20010523/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L45          45 SEA FILE=EMBASE ABB=ON  GROBETA OR GRO BETA
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L47        8719 SEA FILE=EMBASE ABB=ON  GRANULOCYTE COLONY STIMULATING
                FACTOR/CT
L48        3289 SEA FILE=EMBASE ABB=ON  COLONY STIMULATING FACTOR/CT
L49           1 SEA FILE=EMBASE ABB=ON  L45 AND (L47 OR L48)


L45          45 SEA FILE=EMBASE ABB=ON  GROBETA OR GRO BETA
L50        2336 SEA FILE=EMBASE ABB=ON  ANTIMICROBIAL THERAPY/CT
L51       17928 SEA FILE=EMBASE ABB=ON  ANTIINFECTIVE AGENT/CT
L52       64028 SEA FILE=EMBASE ABB=ON  ANTIBIOTIC AGENT/CT
L53       37843 SEA FILE=EMBASE ABB=ON  ANTIMICROBIAL ACTIVITY+NT/CT
L54       10398 SEA FILE=EMBASE ABB=ON  ANTIFUNGAL AGENT/CT
L55        1019 SEA FILE=EMBASE ABB=ON  FUNGICIDE/CT
L56         412 SEA FILE=EMBASE ABB=ON  ANTIMYCOBACTERIAL AGENT/CT
L57         527 SEA FILE=EMBASE ABB=ON  LEPROSTATIC AGENT/CT
L58        6076 SEA FILE=EMBASE ABB=ON  TUBERCULOSTATIC AGENT/CT
L59           2 SEA FILE=EMBASE ABB=ON  ANTISPIROCHETAL AGENT/CT
L60           5 SEA FILE=EMBASE ABB=ON  ANTITREPONEMAL AGENT/CT
L61       14472 SEA FILE=EMBASE ABB=ON  ANTIVIRUS AGENT/CT
L62           1 SEA FILE=EMBASE ABB=ON  L45 AND ((L50 OR L51 OR L52 OR L53 OR
                L54 OR L55 OR L56 OR L57 OR L58 OR L59 OR L60 OR L61))


L76           2 L49 OR L62

=> fil caba jic biosis biotechno confsci biotechds scisearch wpids
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=> d que l72; d que l73; s l72 or l73
L63         189 SEA GROBETA OR GRO BETA
L64         641 SEA GCSF
L65      136759 SEA COLONY STIMULATING OR CSF
L71       32665 SEA (G OR GRANULOCYTE)(W) L65
L72          15 SEA L63 AND (L64 OR L71)
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L63          189 SEA GROBETA OR GRO BETA
L66       216758 SEA MYCOS!S OR FUNGICID? OR ANTIFUNG? OR ANTI FUNG?
L67       605508 SEA ANTIBACTER? OR ANTIBIOT? OR ANTIMICROB? OR ANTIINFECT? OR
                 BACTERI!STAT?
L68        43253 SEA ANTI(W)(BACTER? OR BIOT? OR MICROB? OR INFECT?)
L69       128859 SEA ANTIVIR? OR ANTI(W)(VIRAL? OR VIRUS?) OR VIRUCID?
L73           15 SEA L63 AND ((L66 OR L67 OR L68 OR L69))


L77           28 L72 OR L73

=> dup rem l75,l74,l76,l77
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PROCESSING COMPLETED FOR L75
PROCESSING COMPLETED FOR L74
PROCESSING COMPLETED FOR L76
PROCESSING COMPLETED FOR L77
L78           31 DUP REM L75 L74 L76 L77 (13 DUPLICATES REMOVED)
                 ANSWERS '1-3' FROM FILE MEDLINE
                 ANSWERS '4-14' FROM FILE HCAPLUS
                 ANSWER '15' FROM FILE EMBASE
                 ANSWERS '16-21' FROM FILE BIOSIS
                 ANSWER '22' FROM FILE BIOTECHNO
                 ANSWER '23' FROM FILE SCISEARCH
                 ANSWERS '24-31' FROM FILE WPIDS

=> d ibib ab l78 1-31; fil hom

L78  ANSWER 1 OF 31  MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:   2001227303     MEDLINE
DOCUMENT NUMBER:    21134491   PubMed ID: 11238087
TITLE:              Rapid mobilization of murine hematopoietic stem cells with
                    enhanced engraftment properties and evaluation of
                    hematopoietic progenitor cell mobilization in rhesus
```

monkeys by a single injection of SB-251353, a specific truncated form of the human CXC chemokine **GRObeta**.

AUTHOR: King A G; Horowitz D; Dillon S B; Levin R; Farese A M; MacVittie T J; Pelus L M

CORPORATE SOURCE: Department of Molecular Virology and Host Defense, SmithKline Beecham Pharmaceuticals, Collegeville, PA 19426-0989, USA.. andrew_g_king@sbphrd.com

SOURCE: BLOOD, (2001 Mar 15) 97 (6) 1534-42.
Journal code: A8G; 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200104

ENTRY DATE: Entered STN: 20010502
Last Updated on STN: 20010502
Entered PubMed: 20010312
Entered Medline: 20010426

AB SB-251353 is an N-terminal truncated form of the human CXC chemokine **GRObeta**. Recombinant SB-251353 was profiled in murine and rhesus monkey peripheral blood stem cell mobilization and transplantation models. SB-251353 rapidly and transiently mobilized hematopoietic stem cells and neutrophils into the peripheral blood after a single subcutaneous injection. Transplantation of equivalent numbers of hematopoietic stem cells mobilized by SB-251353 into lethally irradiated mice resulted in faster neutrophil and platelet recovery than stem cells mobilized by granulocyte colony-stimulating factor (G-CSF). A single injection of SB-251353 in combination with 4 days of G-CSF administration resulted in augmented stem and progenitor cell mobilization 5-fold greater than G-CSF alone. Augmented stem cell mobilization could also be demonstrated in mice when a single injection of SB-251353 was administered with only one-day treatment with G-CSF. In addition, SB-251353, when used as a single agent or in combination with G-CSF, mobilized long-term repopulating stem cells capable of hematopoietic reconstitution of lethally irradiated mice. In rhesus monkeys, a single injection of SB-251353 induced rapid increases in peripheral blood hematopoietic progenitor cells at a 50-fold lower dose than in mice, which indicates a shift in potency. These studies provide evidence that the use of SB-251353 alone or in combination with G-CSF mobilizes hematopoietic stem cells with long-term repopulating ability. In addition, this treatment may (1) reduce the number of apheresis sessions and/or amount of G-CSF required to collect adequate numbers of hematopoietic stem cells for successful peripheral blood cell transplantation and (2) improve hematopoietic recovery after transplantation.

L78 ANSWER 2 OF 31 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 2000192038 MEDLINE

DOCUMENT NUMBER: 20192038 PubMed ID: 10725737

TITLE: Identification of unique truncated KC/**GRO beta** chemokines with potent hematopoietic and anti-infective activities.

AUTHOR: King A G; Johanson K; Frey C L; DeMarsh P L; White J R; McDevitt P; McNulty D; Balcarek J; Jonak Z L; Bhatnagar P K; Pelus L M

CORPORATE SOURCE: Department of Molecular Virology, Project Management, Microbial Infectivity, Molecular Genetics, SmithKline Beecham Pharmaceuticals, Collegeville, PA 19426, USA.. Andrew_G_King@sbphrd.com

SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Apr 1) 164 (7) 3774-82.
Journal code: IFB; 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000512
Last Updated on STN: 20000512
Entered Medline: 20000504

AB SK&F 107647, a previously described synthetic immunomodulatory peptide, indirectly stimulates bone marrow progenitor cells and phagocytic cells, and enhances host defense effector mechanisms in bacterial and fungal infection models in vivo. In vitro, SK&F 107647 induces the production of a soluble mediator that augments colony forming cell (CFU-GM) formation in the presence of CSFs. In this paper we purified and sequenced the stromal cell-derived hematopoietic synergistic factors (HSF) secreted from both murine and human cell lines stimulated with SK&F 107647. Murine HSF is an N-terminal 4-aa truncated form of the CXC chemokine, KC, while human HSF was identified as an N-terminal 4-aa truncated form of the CXC chemokine, **GRO beta**. In comparison to their full-length forms, truncated KC and truncated **GRO beta** were 10 million times more potent as synergistic growth stimulants for CFU-GM. Enhanced potency of these novel truncated chemokines relative to their full-length forms was also demonstrated in respiratory burst assays, CD11b Ag expression, and intracellular killing of the opportunistic pathogen, Candida albicans. Administration of truncated KC significantly enhanced survival of mice lethally infected with C. albicans. The results reported herein delineate the biological mechanism of action of SK&F 107647, which functions via the induction of unique specific truncated forms of the chemokines KC and **GRO beta**. To our knowledge, this represents the first example where any form of KC or **GRO beta** were purified from marrow stromal cells. Additionally, this is the first demonstration of in vivo efficacy of a CXC chemokine in an animal infectious fungal disease model.

L78 ANSWER 3 OF 31 MEDLINE
ACCESSION NUMBER: 93224751 MEDLINE
DOCUMENT NUMBER: 93224751 PubMed ID: 7682242
TITLE: Comparative analysis of the human macrophage inflammatory protein family of cytokines (chemokines) on proliferation of human myeloid progenitor cells. Interacting effects involving suppression, synergistic suppression, and blocking of suppression.
AUTHOR: Broxmeyer H E; Sherry B; Cooper S; Lu L; Maze R; Beckmann M P; Cerami A; Ralph P
CORPORATE SOURCE: Department of Medicine (Hematology/Oncology), Indiana University School of Medicine, Indianapolis 46202.
CONTRACT NUMBER: R01 HL46549 (NHLBI)
R01 HL49202 (NHLBI)
R37 CA36464 (NCI)
+
SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Apr 15) 150 (8 Pt 1) 3448-58.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930521
Last Updated on STN: 19970203
Entered Medline: 19930512

AB Macrophage inflammatory protein (MIP)-1 alpha, part of a family termed

chemokines, has been implicated in suppression of hemopoietic stem and progenitor cell proliferation. The chemokine family has been organized into two subgroups with MIP-1 alpha, MIP-1 beta, macrophage chemotactic and activating factor (MCAF) and RANTES belonging to one subgroup, and GRO-alpha, MIP-2 alpha (**GRO-beta**), MIP-2 beta (GRO-gamma), platelet factor 4 (PF4), IL-8, and neutrophil activating peptide (NAP)-2 belonging to the other. These molecules were evaluated for effects on colony formation by human bone marrow multipotential (CFU-GEMM), erythroid (BFU-E) and granulocyte-macrophage (CFU-GM) progenitor cells. None of the chemokines stimulated colony formation in the absence of CSF, or influenced colony formation stimulated by a single growth factor such as granulocyte-macrophage-CSF or erythropoietin. However, MIP-1 alpha, MIP-2 alpha, PF4, IL-8, and MCAF suppressed in dose-response fashion colony formation of immature subsets of myeloid progenitor cells stimulated by GM-CSF plus steel factor. Effects were apparent on low density and CD34 HLA-DR(+)-sorted marrow cells in which up to 88.4% of the cells were composed of progenitor cells, suggesting direct effects on the progenitors themselves. Up to 2500-fold less of each chemokine could be used to demonstrate synergistic suppression when any two of these five chemokines were used together at low concentrations, effects also apparently directly on the progenitors. In contrast, MIP-1 beta, MIP-2 beta, GRO-alpha, NAP-2, and RANTES were not suppressive nor did they synergize with MIP-1 alpha, MIP-2 alpha, PF4, IL-8, or MCAF to suppress. However, a fivefold excess of MIP-1 beta blocked the suppressive effects of MIP-1 alpha. Similarly, a fivefold excess of either MIP-2 beta or GRO-alpha blocked the suppressive effects of IL-8 and PF4. These suppressing, synergizing and blocking effects may be of relevance to blood cell regulation.

L78 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2001 ACS DUPLICATE 5
ACCESSION NUMBER: 1998:719289 HCAPLUS
DOCUMENT NUMBER: 130:3079
TITLE: Method of treating sepsis
INVENTOR(S): Demarsh, Peter Lawrence; Johanson, Kyung O.
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848828	A1	19981105	WO 1998-US8742	19980429
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6042821	A	20000328	US 1997-846966	19970429
EP 981361	A1	20000301	EP 1998-920047	19980429
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				

PRIORITY APPLN. INFO.:
US 1997-846966 A 19970429
US 1995-7425 P 19951121
WO 1996-US18616 A2 19961120
WO 1998-US8742 W 19980429

AB The invention relates to the method of preventing and treating sepsis using chemokines selected from mature or modified KC [SEQ ID NO:1], gro.alpha. [SEQ ID NO:2], **gro.beta**. [SEQ ID NO:3] or gro.gamma. [SEQ ID NO:4] or multimers thereof, alone or in conjunction with an anti-infective agent. This invention also relates to a new **gro.beta**. dimer chemokine.

REFERENCE COUNT: 5
REFERENCE(S): (1) Cao; J Exp Med 1995, V182, P2069 HCAPLUS
(2) Cuenca; Surgical Oncology 1992, V1, P323 MEDLINE
(3) Laterveer; Blood 1996, V87(2), P781 HCAPLUS
(4) Rollins; US 5459128 A 1995 HCAPLUS
(5) Stoeckle, M; Nucleic Acids Research 1991, V19(4), P917 HCAPLUS

L78 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:707004 HCAPLUS
DOCUMENT NUMBER: 133:271639
TITLE: Method and pharmaceutical composition for wound healing
INVENTOR(S): Blumenfeld, Israel; Ullmann, Yehuda; Laufer, Dov; Livne, Erela
PATENT ASSIGNEE(S): Technion Research and Development Foundation Ltd., Israel
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057902	A1	20001005	WO 2000-IL173	20000316

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IL 1999-129180 A 19990325
AB A method of treating a wound is provided. The method is effected by topically applying a chemokine to the wound. A pharmaceutical compn. for topically treating a wound is further provided. The compn. contains an effective concn. of a chemokine and a pharmaceutically acceptable carrier.
REFERENCE COUNT: 2
REFERENCE(S): (1) Herrmann; US 6100387 A 2000 HCAPLUS
(2) Strieter; US 5871723 A 1999 HCAPLUS

L78 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:84648 HCAPLUS
DOCUMENT NUMBER: 132:141941
TITLE: Conjugates and fusion proteins for treating secondary tissue damage and other inflammatory conditions and disorders
INVENTOR(S): Mcdonald, John R.; Coggins, Philip J.
PATENT ASSIGNEE(S): Osprey Pharmaceuticals Limited, Can.
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000004926	A2	20000203	WO 1999-CA659	19990721
WO 2000004926	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9948918	A1	20000214	AU 1999-48918	19990721
EP 1098664	A2	20010516	EP 1999-932572	19990721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-120523 A2 19980722
WO 1999-CA659 W 19990721

AB Conjugates contg. as a ligand a chemokine receptor-targeting agent, such as chemokines, and a targeted agent, such as a toxin are provided. These conjugates are used to treat inflammatory responses assocd. with activation, proliferation and migration of immune effector cells, including leukocyte cell types, neutrophils, macrophages, and eosinophils. The conjugates provided herein are used to lessen or inhibit these processes to prevent or at least lessen the resulting secondary effects. In particular, the conjugates are used to target toxins to receptors on secondary tissue damage-promoting cells. The ligand moiety can be selected to deliver the cell toxin to such secondary tissue damage-promoting cells as mononuclear phagocytes, leukocytes, natural killer cells, dendritic cells, and T and B lymphocytes, thereby suppressing the proliferation, migration, or physiol. activity of such cells. Among preferred conjugates are fusion proteins having a chemokine, or a biol. active fragment thereof, as the ligand moiety linked to a cell toxin via a peptide linker of from 2 to about 60 amino acid residues.

L78 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:205095 HCAPLUS
DOCUMENT NUMBER: 132:250026
TITLE: Method of treating sepsis with chemokines
INVENTOR(S): Demarsh, Peter Lawrence; Johanson, Kyung Oh
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: U.S., 9 pp., Cont.-in-part of WO9719173.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

US 6042821	A	20000328	US 1997-846966	19970429
WO 9719173	A1	19970529	WO 1996-US18616	19961120
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9803524	A	19990111	ZA 1998-3524	19980428
WO 9848828	A1	19981105	WO 1998-US8742	19980429
W: CA, JP, US				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 981361 A1 20000301 EP 1998-920047 19980429
R: BE, CH, DE, ES, FR, GB, IT, LI, NL
PRIORITY APPLN. INFO.: US 1995-7425 P 19951121
WO 1996-US18616 A2 19961120
US 1997-846966 A 19970429
WO 1998-US8742 W 19980429

AB The invention relates to the method of preventing and treating sepsis using chemokines selected from mature or modified KC [SEQ ID NO: 1], gro.alpha. [SEQ ID NO: 2], **gro.beta.** [SEQ ID NO: 3] or gro.gamma. [SEQ ID NO: 4] or multimers thereof, alone or in conjunction with an anti-infective agent. This invention also relates to a new **gro.beta.** dimer chemokine. The chemokine may be administered in conjunction with an anti-infective agent, e.g. gentamicin, augmentin or ceftazidime.

REFERENCE COUNT: 6
REFERENCE(S):
(1) Arturson, G; Burns 1985, V11, P309 MEDLINE
(2) Bossink; Blood 1995, V86(10), P3841 HCAPLUS
(3) Bowie; Science 1990, V247, P1306 HCAPLUS
(5) Driscoll, K; Experimental Lung Research 1994, V20, P473 HCAPLUS
(6) Jansen; The Journal of Infectious Diseases 1995, V171, P1640 MEDLINE
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:468560 HCAPLUS
DOCUMENT NUMBER: 131:116232
TITLE: Preparation of benzoisothiazoline S,S-dioxide derivatives as interleukin-8 (IL-8) receptor antagonists
INVENTOR(S): Bryan, Deborah Lynne; Widdowson, Katherine L.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936069	A1	19990722	WO 1999-US1029	19990115

W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9922341	A1	19990802	AU 1999-22341	19990115
EP 1039903	A1	20001004	EP 1999-902334	19990115

R: BE, CH, DE, ES, FR, GB, IT, LI, NL
PRIORITY APPLN. INFO.: US 1998-71653 P 19980116
WO 1999-US1029 W 19990115
OTHER SOURCE(S): MARPAT 131:116232

AB This invention relates to novel compds. of formula [I; A = (un)substituted CH2; R = NHC(:NX)NH(CR13R14)v-Z; X = cyano, OR11, COR11, CO2R11, SO2R22, R23, (un)substituted CONH2; Z = fused Ph, optionally substituted heteroaryl, optionally substituted C5-8 cycloalkyl, optionally substituted

C1-10 alkyl, optionally substituted C2-10 alkenyl, optionally substituted C2-10 alkynyl; m = an integer having a value of 1 or 3; v = 0, or an integer having a value of 1 to 4; R1 is independently selected from hydrogen, halogen, nitro, cyano, halo-substituted C1-10 alkyl, C1-10 alkyl, C2-10 alkenyl, C1-10 alkoxy, halo-substituted C1-10 alkoxy, (CR8R8)qS(O)tR4, hydroxy-C1-4 alkyl, aryl, aryl-C1-4 alkyl, aryloxy, aryl-C1-4 alkoxy, heteroaryl, heteroaryl-C1-4 alkyl, heterocyclyl, heterocyclyl-C1-4 alkyl, heteroaryl-C1-4 alkoxy, aryl-C2-10 alkenyl, heteroaryl-C2-10 alkenyl, heterocyclic-C2-10 alkenyl, etc.; wherein R4, R5 = H, optionally substituted C1-4 alkyl, aryl, aryl-C1-4 alkyl, heteroaryl, heteroaryl-C1-4 alkyl, etc.; R8 = H, C1-4 alkyl; q = 0, 1-10; t = 0, 1,2]. These compds. are useful in the treatment of disease states mediated by the chemokine such as interleukin-8 (IL-8), GRO.alpha., **GRO**. **beta**., GRO.gamma., ENA-78, and neutrophil attractant/activation protein (NAP-2) which induce neutrophile shape change, chemotaxis, granule release, and respiratory burst. They are useful for treating psoriasis, atopic dermatitis, arthritis, asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, inflammatory bowel disease, Crohn's disease, ulcerative colitis, stroke, septic shock, endotoxic shock, gram neg. sepsis, toxic shock syndrome, cardiac and renal reperfusion injury, glomerulonephritis, thrombosis, graft vs. host reaction, Alzheimer's disease, allograft rejection, malaria, restenosis, angiogenesis, undesired hematopoietic stem cells release, rhinovirus infections, or periodontal disease or bone resorption disease (no data). Thus, to s stirred mixt. of cyanamide (330 mg, 8.85 mmol) and Huinig's base (0.66 mL) in acetonitrile was added a soln. of N-(1-allyl-4-chloro-2,2-dioxo-2,1-benzisothiazolin-7-yl)-N'-(2-bromophenyl)carbodiimide dropwise. The reaction mixt. was stirred at room temp. for 15 h to give N-(1-allyl-4-chloro-2,2-dioxo-1,2-benzisothiazolin-7-yl)-N'-(2-bromophenyl)-N''-cyanoguanidine. To a mixt. of the latter compd. (80 mg, 0.166 mmol) and sodium borohydride (20 mg, 0.21 mmol) in THF (8 mL) was added at room temp. tetrakistriphenylphosphine palladium[0] (8 mg). The reaction was stirred at room temp. for 2 h to give N-(4-Chloro-1,3-dihydro-2,2-dioxo-1,2-benzisothiazol-7-yl)-N'-(2-bromophenyl)-N''-cyanoguanidine.

REFERENCE COUNT: 2
REFERENCE(S): (1) Nakane; US 5504095 A 1996 HCAPLUS
(2) Schnorrenberg; US 4555511 A 1985 HCAPLUS

L78 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:355743 HCAPLUS
DOCUMENT NUMBER: 131:18015
TITLE: Deamidated chemokine **gro-.beta.** for mobilizing hematopoietic stem cells
INVENTOR(S): King, Andrew G.; Qian, Yanqiu
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, UK
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926645	A1	19990603	WO 1998-US24884	19981120

W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9915962 A1 19990615 AU 1999-15962 19981120
EP 1033997 A1 20000913 EP 1998-960346 19981120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI
ZA 9810775 A 19990526 ZA 1998-10775 19981125
PRIORITY APPLN. INFO.: US 1997-999804 A 19971126
WO 1998-US24884 W 19981120

AB A method of mobilizing hematopoietic stem cells from the bone marrow to the peripheral circulation is provided by administering to an animal an effective amt. of mature, modified or multimeric forms of KC, **gro .beta.**, gro.alpha. or gro.gamma..

REFERENCE COUNT: 3
REFERENCE(S): (1) Bongers; Int J Peptide Protein Res 1992, V39, P364 HCAPLUS
(2) Friedman; Int J Peptide Protein Res 1991, V37, P14 HCAPLUS
(3) Sager; US 5154921 A 1992 HCAPLUS

L78 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:194178 HCAPLUS
DOCUMENT NUMBER: 130:236476
TITLE: Chemokine-derived peptides, peptide variants, derivatives and analogs for modulation of inflammatory responses
INVENTOR(S): Grainger, David J.; Tatalick, Lauren Marie; Kanaly, Suzanne T.
PATENT ASSIGNEE(S): Neorx Corporation, USA
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9912968	A2	19990318	WO 1998-US19052	19980911
WO 9912968	A3	19990729		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9893153	A1	19990329	AU 1998-93153	19980911
EP 1012187	A2	20000628	EP 1998-946057	19980911

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1997-927939 A2 19970911
WO 1998-US19052 W 19980911

AB The authors disclose the identification and characterization of chemokine-derived peptides, substituted variants and isosteres, and peptidic mimics that exhibit agonistic and antagonistic activity for chemokine receptors. In one example, a peptide derived from a conserved region of human monocyte chemoattractant protein-1 (MCP-1) was shown to inhibit the migration of the THP-1 cell line in response to MIP-1.alpha., MCP-1, SDF-1.alpha., and IL-8. Thus, inhibition was both specific and general. In addn., cyclic and reverse D-enantiomeric analogs of the

peptide exhibited improved antagonistic activity. In a second example, a peptide derived from a non-conserved portion of MCP-1 was shown to inhibit CXCR4-mediated infection of Jurkat cells by HIV.

L78 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:672475 HCAPLUS
DOCUMENT NUMBER: 129:301695
TITLE: Chemokines that inhibit immunodeficiency virus infection and methods based thereon
INVENTOR(S): Devico, Anthony L.; Gallo, Robert C.; Garzino-Demo, Alfredo
PATENT ASSIGNEE(S): University of Maryland Biotechnology Institute, USA
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842354	A1	19981001	WO 1998-US5987	19980326
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6214540	B1	20010410	US 1997-826133	19970326
AU 9865875	A1	19981020	AU 1998-65875	19980326

PRIORITY APPLN. INFO.: US 1997-826133 A 19970326
WO 1998-US5987 W 19980326

AB Therapeutic compns. and methods are provided for treating and preventing infection by an immunodeficiency virus, particularly HIV, using chemokine proteins, nucleic acids, and/or derivs. or analogs thereof (no data). These compns. inhibit replication and/or infection by HIV, preferably by binding to .gtoreq.2 chemokine receptors. The nucleic acids may be used for gene therapy. Chemokines with anti-HIV activity are identified by comparing the ability to isolate HIV from HIV-pos. cells exposed vs. not exposed to the chemokine or to sets of chemokines.

L78 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:440267 HCAPLUS
DOCUMENT NUMBER: 127:60613
TITLE: Chemokines and chemokine analogs for prevention and treatment of sepsis
INVENTOR(S): Demarsh, Peter Lawrence; Johanson, Kyung O.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Demarsh, Peter Lawrence; Johanson, Kyung O.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719173	A1	19970529	WO 1996-US18616	19961120
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

AU 9710209	A1	19970611	AU 1997-10209	19961120	
EP 871732	A1	19981021	EP 1996-940554	19961120	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI					
JP 2000504310	T2	20000411	JP 1997-519868	19961120	
US 6042821	A	20000328	US 1997-846966	19970429	
PRIORITY APPLN. INFO.:			US 1995-7425	P	19951121
			WO 1996-US18616	W	19961120

AB A method of preventing and treating sepsis using chemokines selected from monomers or oligomers of mature or modified KC, gro.alpha., **gro.beta.**, or gro.gamma., either alone or in conjunction with an anti-infective agent is described. Manuf. of the proteins in Escherichia coli is described. The effectiveness of the chemokines was tested in a rat model in which Escherichia coli-contg. fibrin-thrombin clots were implanted. In control expts., 8 of 25 rats treated with gentamicin only survived. When rats were treated, either prophylactically or therapeutically, with 5-72-chemokine KC at 33 or 100 fg/kg, the survival rate increased to 17-18/25.

L78 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1997:374859 HCAPLUS
DOCUMENT NUMBER:	126:342449
TITLE:	Intercrines or chemokines for mobilizing hematopoietic stem cells
INVENTOR(S):	Pelus, Louis Martin; King, Andrew Garrison
PATENT ASSIGNEE(S):	Smithkline Beecham Corporation, USA; Pelus, Louis Martin; King, Andrew Garrison
SOURCE:	PCT Int. Appl., 31 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9715595	A1	19970501	WO 1996-US17074	19961024
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9608896	A	19970424	ZA 1996-8896	19961023
AU 9675209	A1	19970515	AU 1996-75209	19961024
AU 712235	B2	19991104		
EP 866806	A1	19980930	EP 1996-937739	19961024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
CN 1205708	A	19990120	CN 1996-199238	19961024
BR 9611173	A	19990330	BR 1996-11173	19961024
JP 11512747	T2	19991102	JP 1996-516787	19961024
NO 9801818	A	19980617	NO 1998-1818	19980423
PRIORITY APPLN. INFO.:			US 1995-547262	A2 19951024
			WO 1996-US17074	W 19961024

AB A method of mobilizing hematopoietic stem cells from the bone marrow to the peripheral circulation is provided by administering to an animal an effective amt. of nature, modified or multimeric forms of chemokines, e.g. KC, **gro.beta.**, gro.alpha. or gro.gamma.. Medicament contg. the chemokine and growth factor or other hematopoietic regulatory biomol. is used for treating patients receiving peripheral blood

hematopoietic stem cell transplantation, or for pretreating patient before receiving chemotherapeutic agent to harvest hematopoietic stem cells for reinfusion.

L78 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:501470 HCAPLUS
DOCUMENT NUMBER: 125:140564
TITLE: Mobilization of hematopoietic cells
INVENTOR(S): McCourt, Matthew John; Wood, Lars Michael; Hunter, Michael George; Czaplewski, Lloyd George
PATENT ASSIGNEE(S): British Biotech Pharmaceuticals Limited, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9619234	A1	19960627	WO 1995-GB2929	19951215
W: AU, BR, CA, CN, CZ, DE, FI, GB, HU, JP, KR, NO, NZ, PL, RU, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9641852	A1	19960710	AU 1996-41852	19951215
EP 800402	A1	19971015	EP 1995-940384	19951215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				

PRIORITY APPLN. INFO.: GB 1994-26012 19941222
WO 1995-GB2929 19951215

AB The combination of CxC chemokine such as GRO and a hematopoiesis priming agent such as a colony stimulating factor promotes release and mobilization of hematopoietic cells into the bloodstream. The combination of chemokine and hematopoiesis priming agent is useful for treating leukopenia, myelo-dysplastic syndrome, acute or chronic microbial or fungal or parasitic infection, and for harvesting blood cell for peripheral blood cell transplantation after patient undergone chemo- or radio-therapy.

L78 ANSWER 15 OF 31 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96298522 EMBASE
DOCUMENT NUMBER: 1996298522
TITLE: [Occurrence of mycobacteria between 1985 and 1995 in the Dusseldorf area - Pattern of resistance, distribution and assignment to different patient groups].
AUFTRETEN VON MYKOBAKTERIEN ZWISCHEN 1985 UND 1995 IM **GRO.beta.**RAUM DUSSELDORF - RESISTENZENTWICKLUNG, VERTEILUNG UND ZUORDNUNG ZU VERSCHLEDEN PATIENTENKOLLEKTIVEN.
AUTHOR: Schmitz F.-J.; Haupt C.; Kitzrow M.; Novak R.; Idel H.; Hadding U.; Heinz H.P.
CORPORATE SOURCE: Inst Medizinische Microbiol. Virol., Heinrich-Heine-Univ. Dusseldorf, Universitatsstrasse 1,40225 Dusseldorf, Germany
SOURCE: Klinisches Labor, (1996) 42/9 (731-744).
ISSN: 0941-2131 CODEN: KLLAEA
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: German; English

AB All data collected over a period of 11 years by the Department of Microbiology and Virology of Dusseldorf University with regard to mycobacterial first isolates (M. tuberculosis and MOTT) and their patterns of resistance, distribution and assignment to different patient populations were analyzed in the present study. The data show that the relationship between M. tuberculosis and MOTT has shifted in favor of the latter during these years. Between 1985 and 1995 the resistance of isolated mycobacteria to various tuberculostatic drugs (isoniazid, ethambutol, streptomycin, rifampicin, prothionamide, pyracinamide) did not increase. The share of multiresistant M. tuberculosis isolates (resistant to two antibiotics or more) among all detected mycobacteria ranged from 5% to 15% during these years, the average being 8.4%. No increase of combined single resistance was found among the group of multiresistant mycobacterial isolates, and neither M. tuberculosis nor MOTT revealed a significant increase of resistance. Allocation of the M. tuberculosis isolates to patients of different nationalities (Germans/foreigners) did not reveal a clear tendency towards an increased occurrence in one or the other of these two groups, neither when all isolates were considered together nor when the multiresistant isolates were considered separately. No statistically significant difference was observed during the last three years concerning the age of patients with positive M. tuberculosis or MOTT isolates. Analysis of the sample material submitted from 1985 until 1995 showed that typical mycobacteria as well as MOTT were most frequently detectable in sputum. Up to 33% of all M. tuberculosis isolates were found in patients with co-existing HIV infection, whereas MOTT were associated with HIV infection in up to 65% of cases.

L78 ANSWER 16 OF 31 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
ACCESSION NUMBER: 2000:162589 BIOSIS
DOCUMENT NUMBER: PREV200000162589
TITLE: Potency of ligands correlates with affinity measured against agonist and inverse agonists but not against neutral ligand in constitutively active chemokine receptor.
AUTHOR(S): Rosenkilde, Mette M. (1); Schwartz, Thue W.
CORPORATE SOURCE: (1) Laboratory for Molecular Pharmacology, Panum Institute 18.6, Blegdamsvej 3, DK-2200, Copenhagen Denmark
SOURCE: Molecular Pharmacology., (March, 2000) Vol. 57, No. 3, pp. 602-609.
ISSN: 0026-895X.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB ORF-74, a 7TM receptor oncogene encoded by human herpes virus 8, shows 50% constitutive activity in stimulating phosphatidylinositol turnover and binds a large variety of CXC chemokines. These endogenous ligands cover a full spectrum of pharmacological properties with growth-related oncogene (GRO)-alpha and -gamma functioning as full agonists; **GRObeta** as a partial agonist; interleukin (IL)-8, neutrophil-activating peptide (NAP)-2, and epithelial cell-derived activating peptide (ENA)-78 as neutral ligands; **granulocyte colony-stimulating** factor (GCP)-2 as a partial inverse agonist; and interferon-gamma inducible protein (IP)-10 and stromal cell-derived factor (SDF)-1alpha as full inverse agonists. The affinity for the agonists was independent of whether it was determined in competition binding against the agonist 125I-GROalpha, against the inverse agonist 125I-IP-10, or against the neutral ligand 125I-IL-8. Similarly, the affinities of the inverse agonists were within 1 order of magnitude independent of the choice of radioligand. In contrast, the neutral ligands IL-8, NAP-2, and ENA-78, which all displaced 125I-IL-8 with single-digit nanomolar affinity showed up to 1000-fold lower affinity against both the radioactive agonist and against the radioactive inverse agonist. A close correlation was

observed between the EC50 values for the ligands and their IC50 values measured against either radioactive agonist or radioactive inverse agonist, but a poor correlation was found to the IC50 value measured against the neutral ligand. It is concluded that in ORF-74, ligands compete for binding more according to pharmacological property than to structural homology and that both agonists and inverse agonists, in contrast to neutral ligands, apparently bind with high affinity either to a common conformation of the receptor or to readily interconvertible states, not available for the neutral ligands.

L78 ANSWER 17 OF 31 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
ACCESSION NUMBER: 2000:85195 BIOSIS
DOCUMENT NUMBER: PREV200000085195
TITLE: Nuclear magnetic resonance solution structure of truncated human **GRObeta** (5-73) and its structural comparison with CXC chemokine family members GROalpha and IL-8.
AUTHOR(S): Qian, Yan Qiu (1); Johanson, Kyung O.; McDevitt, Patrick
CORPORATE SOURCE: (1) Department of Physical and Structural Chemistry, SmithKline Beecham-Pharmaceuticals, UW-2940, King of Prussia, PA, 19406 USA
SOURCE: Journal of Molecular Biology, (Dec. 17, 1999) Vol. 294, No. 5, pp. 1065-1072.
ISSN: 0022-2836.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The three-dimensional structure of a novel four amino acid truncated form of the CXC chemokine **GRObeta** (5-73) isolated from bone marrow stromal cells with potent hematopoietic and **anti-infective** activities has been determined by two-dimensional 1H nuclear magnetic resonance (NMR) spectroscopy in solution. On the basis of 1878 upper distance constraints derived from nuclear Overhauser effects (NOE) and 314 dihedral angle constraints, a group of 20 conformers representing the solution structure of the human **GRObeta** (5-73) was computed with the program DYANA. At the concentrations used for NMR study, **GRObeta** (5-73) forms a dimer in solution that is architectured by a six-stranded antiparallel beta-sheet (residues 25 to 29, 39 to 44, 49 to 52) and a pair of helices (residues 58 to 68) with 2-fold symmetry, while the C terminus of the protein is disordered. The average of the pairwise root-mean-square deviations of individual NMR conformers relative to the mean coordinates for the backbone atoms N, Calpha and C' of residues 5 to 68 is 0.47 ANG. Overall, the global fold of **GRObeta** (5-73) is similar to that of the previously reported NMR structure of GROalpha and the NMR and X-ray structures of interleukin-8. Among these three CXC chemokines, **GRObeta** (5-73) is most similar in structure to GROalpha. Significant differences between **GRObeta** (5-73), GROalpha and interleukin-8 are in the N-terminal loop comprising residues 12 to 19. The N-terminal arm containing the conserved ELR motif and the loop of residues 30 to 38 containing the GPH motif are different among these three CXC chemokines. The structural differences in these two regions may be responsible for the specificity of the receptor binding and biological activity of different chemokines.

L78 ANSWER 18 OF 31 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:264641 BIOSIS
DOCUMENT NUMBER: PREV200100264641
TITLE: Differential SOCS gene expression in two human lung carcinoma lines.
AUTHOR(S): Szente, Brian E. (1); Feege, Maureen (1); Jackson, Jeffrey R. (1)

CORPORATE SOURCE: (1) SmithKline Beecham Pharmaceuticals, 709 Swedeland Road, UW2532, King of Prussia, PA, 19406 USA
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1053. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The Suppressors of Cytokine Signaling (SOCS) family of proteins was first characterized based on the ability of SOCS1 to inhibit the activity of the JAK-Stat signaling pathways induced in response to IL-4, IL-6, LIF, and **G-CSF**. Here we describe the differential expression of additional SOCS family genes, SOCS-4, SOCS-5 and SOCS-6, in two human lung carcinoma lines, NCI-H460 and NCI-H520. The NCI-H460 line, which is a large cell cancer, constitutively expresses SOCS-4, SOCS-5 and SOCS-6 in culture. On the other hand, the NCI-H520 line, which is a squamous cell carcinoma, does not constitutively express this same set of SOCS genes. An exchange of conditioned medium between confluent cultures of these two carcinoma lines results in the loss of SOCS-4, SOCS-5 and SOCS-6 expression in NCI-H460 and a corresponding gain of SOCS-5 and SOCS-6 expression in the NCI-H520 line. Transcriptional profiling of the genes for cytokines/growth factors and their receptors in these two lines revealed significant differences in the expression of a number of chemokines. Members of the C-X-C family of chemokines, including IL-8 and **Grobeta**, were more highly expressed in the NCI-H460 line than in the NCI-H520 line. Specific stimulation of the NCI-H520 line with **Grobeta** resulted in the increased expression of the genes for SOCS-5 and SOCS-6, while stimulation with IL-8 also led to the expression of SOCS-4. This is the first observation of chemokine stimulation leading to SOCS gene expression, and may indicate an expanded regulatory repertoire for the SOCS family.

L78 ANSWER 19 OF 31 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:45082 BIOSIS
DOCUMENT NUMBER: PREV200000045082
TITLE: Multi-lineage effects of truncated **GRObeta** (SB-251353) in combination with hematopoietic growth factors in chemotherapy-induced myelosuppression models.
AUTHOR(S): King, A. G. (1); Averill, L. (1); Dillon, S. (1); Horowitz, D. (1); Pelus, L. M. (1); Levin, R. (1)
CORPORATE SOURCE: (1) Molecular Virology and Host Defense, SmithKline Beecham Pharmaceuticals, Collegeville, PA USA
SOURCE: Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 50a-51a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L78 ANSWER 20 OF 31 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:436378 BIOSIS
DOCUMENT NUMBER: PREV199799735581
TITLE: Human hepatocytes express an array of proinflammatory cytokines after agonist stimulation or bacterial invasion.
AUTHOR(S): Rowell, Diana L.; Eckmann, Lars; Dwinell, Michael B.; Carpenter, Susan P.; Raucy, Judy L.; Yang, Suk-Kyun;

Kagnoff, Martin F. (1)
CORPORATE SOURCE: (1) Dep. Med. 0623D, Univ. Calif. San Diego, 9500 Gilman Dr., La Jolla, CA 92093-0623 USA
SOURCE: American Journal of Physiology, (1997) Vol. 273, No. 2 PART 1, pp. G322-G332.
ISSN: 0002-9513.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Inflammatory cells infiltrate the liver in response to microbial infection or hepatic injury. To assess the potential role hepatocytes may play in initiating or amplifying the acute inflammatory response in the liver, we used three human hepatocyte cell lines and primary human hepatocyte cultures to characterize the repertoire of cytokines that can be expressed and regulated in hepatocytes in response to agonist stimulation or bacterial infection. As reported herein, a proinflammatory cytokine gene program that includes C-X-C and C-C chemokines (interleukin-8 (IL-8), growth related (GRO)-alpha, **GRO-beta**, GRO-gamma, epithelial neutrophil activating peptide-78 (ENA-78), and RANTES) and the cytokines tumor necrosis factor-alpha (TNF-alpha) and macrophage colony stimulating factor was upregulated in human hepatocytes after stimulation with IL-1-alpha or TNF-alpha or bacterial invasion. In contrast, expression of hematopoietic/lymphoid growth factors by the same cells was either downregulated (erythropoietin and stem cell factor) or unchanged (IL-7 and IL-15) in response to the identical stimuli. Hepatocytes did not express cytokines that often are associated with the regulation of antigen-specific immune responses (IL-2, IL-4, IL-5, IL-10, IL-12p40, IL-13, and interferon-gamma) or genes for several other proinflammatory cytokines (IL-1-alpha, IL-6, monocyte chemotactic protein-1 (MCP-1), and MCP-3) or hematopoietic growth factors (**granulocyte colony stimulating** factor, granulocyte macrophage colony stimulating factor, IL-3, and IL-11). Together, these studies suggest that hepatocytes can both initiate and amplify acute inflammatory responses in the liver through the regulated expression and secretion of a specific array of proinflammatory cytokines.

L78 ANSWER 21 OF 31 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:195736 BIOSIS
DOCUMENT NUMBER: PREV199799494939
TITLE: Induction of alpha-chemokines MIP-2 and KC by quinolone **antibiotics** in rat alveolar macrophages in vitro as assayed by RT-PCR.
AUTHOR(S): Rajyaguru, J. M.; Livingston, F. R.; Muszynski, M. J.
CORPORATE SOURCE: Arnold Palmer Hosp. Children Women, Orlando, FL USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1996) Vol. 36, No. 0, pp. 146. Meeting Info.: 36th ICAAC (International Conference of Antimicrobial Agents and Chemotherapy) New Orleans, Louisiana, USA September 15-18, 1996
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L78 ANSWER 22 OF 31 BIOTECHNO COPYRIGHT 2001 Elsevier Science B.V.
ACCESSION NUMBER: 1997:27417941 BIOTECHNO
TITLE: Human hepatocytes express an array of proinflammatory cytokines after agonist stimulation or bacterial invasion
AUTHOR: Rowell D.L.; Eckmann L.; Dwinell M.B.; Carpenter S.P.; Raucy J.L.; Yang S.- K.; Kagnoff M.F.
CORPORATE SOURCE: M.F. Kagnoff, Dept. of Medicine, Univ. of California, 9500 Gilman Dr., San Diego, CA 92093-0623, United States.

Searched by Barb O'Bryen, STIC 308-4291

SOURCE: American Journal of Physiology - Gastrointestinal and Liver Physiology, (1997), 273/2 36-2 (G322-G332), 43 reference(s)
CODEN: APGPDF ISSN: 0193-1857
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Inflammatory cells infiltrate the liver in response to microbial infection or hepatic injury. To assess the potential role hepatocytes may play in initiating or amplifying the acute inflammatory response in the liver, we used three human hepatocyte cell lines and primary human hepatocyte cultures to characterize the repertoire of cytokines that can be expressed and regulated in hepatocytes in response to agonist stimulation or bacterial infection. As reported herein, a proinflammatory cytokine gene program that includes C-X-C and C-C chemokines .cents.interleukin-8 (IL-8), growth related (GRO)-.alpha., **GRO -.beta.**, GRO-.gamma., epithelial neutrophil activating peptide-78 (ENA- 78), and RANTES! and the cytokines tumor necrosis factor-.alpha. (TNF-.alpha.) and macrophage colony stimulating factor was upregulated in human hepatocytes after stimulation with IL-1.alpha. or TNF-.alpha. or bacterial invasion. In contrast, expression of hematopoietic/lymphoid growth factors by the same cells was either down-regulated (erythropoietin and stem cell factor) or unchanged (IL- 7 and IL-15) in response to the identical stimuli. Hepatocytes did not express cytokines that often are associated with the regulation of antigen- specific immune responses (IL-2, IL-4, IL-5, IL-10, IL-12p40, IL-13, and interferon-.gamma.) or genes for several other proinflammatory cytokines .cents.IL-1.alpha., IL-6, monocyte chemotactic protein-1 (MCP-1), and MCP-3! or hematopoietic growth factors (**granulocyte colony stimulating** factor, granulocyte macrophage colony stimulating factor, IL-3, and IL-11). Together, these studies suggest that hepatocytes can both initiate and amplify acute inflammatory responses in the liver through the regulated expression and secretion of a specific array of proinflammatory cytokines.

L78 ANSWER 23 OF 31 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 97:608711 SCISEARCH
THE GENUINE ARTICLE: XQ263
TITLE: Human hepatocytes express an array of proinflammatory cytokines after agonist stimulation or bacterial invasion
AUTHOR: Rowell D L; Eckmann L; Dwinell M B; Carpenter S P; Raucy J L; Yang S K; Kagnoff M F (Reprint)
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, DEPT MED 0623D, 9500 GILMAN DR, LA JOLLA, CA 92093 (Reprint); UNIV CALIF SAN DIEGO, DEPT MED 0623D, LA JOLLA, CA 92093; AGOURON INST, LA JOLLA, CA 92037
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY-GASTROINTESTINAL AND LIVER PHYSIOLOGY, (AUG 1997) Vol. 36, No. 2, pp. G322-G332. Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0193-1857.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Inflammatory cells infiltrate the liver in response to microbial infection or hepatic injury. To assess the potential role hepatocytes may play in initiating or amplifying the acute inflammatory response in the

liver, we used three human hepatocyte cell lines and primary human hepatocyte cultures to characterize the repertoire of cytokines that can be expressed and regulated in hepatocytes in response to agonist stimulation or bacterial infection. As reported herein, a proinflammatory cytokine gene program that includes C-X-C and C-C chemokines [interleukin-8 (IL-8), growth related (GRO)-alpha, **GRO-beta**, GRO-gamma, epithelial neutrophil activating peptide-78 (ENA-78), and RANTES] and the cytokines tumor necrosis factor-alpha (TNF-alpha) and macrophage colony stimulating factor was upregulated in human hepatocytes after stimulation with IL-1 alpha or TNF-alpha or bacterial invasion. In contrast, expression of hematopoietic/lymphoid growth factors by the same cells was either downregulated (erythropoietin and stem cell factor) or unchanged (IL-7 and IL-15) in response to the identical stimuli. Hepatocytes did not express cytokines that often are associated with the regulation of antigen-specific immune responses (IL-2, IL-4, IL-5, IL-10, IL-12p40, IL-13, and interferon-gamma) or genes for several other proinflammatory cytokines [IL-1 alpha, IL-6, monocyte chemotactic protein-1 (MCP-1), and MCP-S] or hematopoietic growth factors (**granulocyte colony stimulating** factor, granulocyte macrophage colony stimulating factor, IL-3, and IL-11). Together, these studies suggest that hepatocytes can both initiate and amplify acute inflammatory responses in the liver through the regulated expression and secretion of a specific array of proinflammatory cytokines.

L78 ANSWER 24 OF 31 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-112195 [12] WPIDS
DOC. NO. CPI: C2001-033271
TITLE: Treatment of chemokine-mediated diseases e.g. malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis and viral diseases such as hepatitis by giving IL-8 receptor antagonists.
DERWENT CLASS: B05
INVENTOR(S): BENSON, G M; WIDDOWSON, K L
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000076515	A1	20001221	(200112)*	EN	45

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AU BA BB BG BR CA CN CZ DZ EE GE GH GM HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ PL RO SG SI SK SL TR TT TZ UA US UZ VN YU ZA

AU 2000058750 A 20010102 (200121)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000076515	A1	WO 2000-US16510	20000615
AU 2000058750	A	AU 2000-58750	20000615

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000058750	A Based on	WO 200076515

PRIORITY APPLN. INFO: US 1999-139673 19990616

AB WO 200076515 A UPAB: 20010302
NOVELTY - Treatment of chemokine-mediated diseases such as malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis, undesired hematopoeitic stem-cell release and diseases caused by respiratory, herpes and hepatitis viruses in which the chemokine binds to an interleukin (IL)-8 alpha or beta receptor by administering phenylurea compounds (I).

DETAILED DESCRIPTION - Chemokine-mediated diseases including malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis, undesired hematopoeitic stem-cell release and diseases caused by respiratory viruses, herpesviruses and hepatitis viruses in which the chemokine binds to an IL-8 alpha or beta receptor are treated by administering phenylurea compounds of formula (I) and their pharmaceutically acceptable salts.

R = (CR8R8)rC(O)2H, (CR8R8)rNHC(O)Ra, (CR8R8)rC(O)NR6'R7', (CR8R8)rNHS(O)2Rb, (CR8R8)rS(O)2NHRc, (CR8R8)rNHRc, (CR8R8)rNHC(X2)NHRb or a tetrazolyl ring;
X, X2 = O or S;

R1, Y = H, halo, nitro, cyano, optionally halo-substituted 1-10C alkyl, 2-10C alkenyl, optionally halo-substituted 1-10C alkoxy, azide, (CR8R8)qS(O)tR4, hydroxy, 1-4C hydroxyalkyl, aryl, aryl-(1-4C) alkyl, aryloxy, aryl-(1-4C) alkyloxy, heteroaryl, heteroarylalkyl, heterocycle, heterocycle-(1-4C) alkyl, heteroaryl-(1-4C) alkyloxy, aryl-(2-10C) alkenyl, heteroaryl-(2-10C) alkenyl, heterocycle-(2-10C) alkenyl, (CR8R8)qNR4R5, 2-10C alkenyl-C(O)NR4R5, (CR8R8)qC(O)NR4R5, (CR8R8)qC(O)NR4R10, S(O)3H, S(O)3R8, (CR8R8)qC(O)R11, 2-10C alkenyl-C(O)R11, 2-10C alkenyl-C(O)OR11(CR8R8)qC(O)OR12, (CR8R8)qOC(O)R11, (CR8R8)qNR4C(O)R11, (CR8R8)qNHS(O)2R17, (CR8R8)qS(O)2NR4R5; or

2R1, 2Y = O(CH2)sO or a 5-6-membered unsaturated ring (all aryl, heteroaryl and heterocyclic containing groups being optionally substituted);
n, m = 1-3;
q = 0-10;
r = 0-4;
s = 1-3;
t = 0-2;

R4, R5 = H, optionally substituted 1-4C alkyl, aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle or heterocycle-(1-4C) alkyl or, together with the N to which they are attached, R4 and R5 form a 5-7-membered ring optionally comprising an additional heteroatom chosen from O, N or S;

R6, R7 = H or 1-4C alkyl; or

NR6R7 = 5-7-membered ring that may optionally contain an additional heteroatom chosen from O, N or S;

R6', R7' = H, 1-4C alkyl, aryl, aryl-(1-4C) alkyl, aryl-(2-4C) alkenyl, heteroaryl, heteroaryl-(1-4C) alkyl, heteroaryl-(2-4C) alkenyl, heterocycle, heterocycle-(1-4C) alkyl or heterocycle-(2-4C) alkenyl (provided that one, but not both, are H);

HET = optionally substituted heteroaryl;

R8 = H or 1-4C alkyl;

R10 = 1-10C alkyl-C(O)2R8;

R11 = H, 1-4C alkyl or optionally substituted aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle, or heterocycle-(1-4C) alkyl;

R12 = H, 1-10C alkyl or optionally substituted aryl or arylalkyl;

R17 = 1-4C alkyl, aryl, arylalkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle or heterocycle-(1-4C) alkyl (all rings being optionally substituted);

Ra = alkyl, aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle, heterocycle-(1-4C) alkyl (all optionally substituted);

Rb = NR6R7, alkyl, aryl, aryl-(1-4C) alkyl, aryl-(2-4C) alkenyl,

heteroaryl, heteroaryl-(1-4C) alkyl, heteroaryl-(2-4C) alkenyl, heterocycle, heterocycle-(1-4C) alkyl, heterocycle-(2-4C) alkenyl or camphor (all optionally substituted);

Rc = alkyl, aryl, aryl-(1-4C) alkyl, aryl-(2-4C) alkenyl, heteroaryl, heteroaryl-(1-4C) alkyl, heteroaryl-(2-4C) alkenyl, heterocycle, heterocycle-(1-4C) alkyl or heterocycle-(2-4C) alkenyl (all optionally substituted by 1-3 of halo, nitro, halo-substituted 1-4C alkyl, 1-4C alkyl, 1-4C alkoxy, NR9C(O)Ra, C(O)NR6R7, S(O)3H or C(O)O-(1-4C) alkyl);

Rd = NR6R7 or alkyl, aryl-(1-4C) alkyl, aryl-(2-4C) alkenyl, heterocycle or heterocycle-(1-4C) alkyl (all optionally substituted);

W = a group of formula (i) or (ii);

E = cyclopentanone (substituted by (Rl)m), indanyl (substituted by Rl) or a group of formula (iii);

asterisk = point of attachment of the ring;

R20 = Wl, or heteroaryl, 5-8C cycloalkyl, 1-10C alkyl, 2-10 C alkenyl or 2-10C alkynyl (all optionally substituted);

Wl = a group of formula (iv) or (v); and

E' = cyclopentanone (substituted by (Y)n), indanyl (substituted by (Y)n) or a group of formula (vi).

ACTIVITY - Protozoacide; antimalarial; vasotropic; antiarteriosclerotic; osteopathic; antiinflammatory; virucide; hepatotropic; antipsoriatic; dermatological; antiarthritic; antiasthmatic; gastrointestinal; antiulcer; bactericidal; nephrotropic; immunostimulant; nootropic; neuroprotective.

MECHANISM OF ACTION - IL-8 alpha receptor antagonist; IL-8 beta receptor antagonist.

USE - (I) are used to treat chemokine-mediated diseases such as malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis, undesired hematopoeitic stem-cell release and diseases caused by respiratory viruses, herpesviruses and hepatitis viruses (claimed). They may be used to treat IL-8, GRO alpha , GRO beta , GRO gamma , NAP-2 and ENA-78-mediated diseases, psoriasis, atopic dermatitis, arthritis, asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, inflammatory bowel disease, Crohn's disease, ulcerative colitis, stroke, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, cardiac and renal reperfusion injury, glomerulonephritis, thrombosis, graft-versus-host disease, Alzheimer's disease and allograft rejections.

Dwg.0/0

L78 ANSWER 25 OF 31 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-112187 [12] WPIDS
DOC. NO. CPI: C2001-033263
TITLE: Treatment of chemokine-mediated diseases e.g. malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis and viral diseases such as hepatitis by giving IL-8 receptor antagonists.
DERWENT CLASS: B05
INVENTOR(S): BENSON, G M; WIDDOWSON, K L
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000076457	A2	20001221	(200112)*	EN	37

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AU BA BB BG BR CA CN CZ DZ EE GE GH GM HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX MZ NO NZ PL RO SG SI SK SL TR TT TZ UA US UZ VN YU ZA

AU 2000060512 A 20010102 (200121)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000076457 A2		WO 2000-US16500	20000615
AU 2000060512 A		AU 2000-60512	20000615

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000060512 A	Based on	WO 200076457

PRIORITY APPLN. INFO: US 1999-139680 19990615

AB WO 200076457 A UPAB: 20010302

NOVELTY - Treatment of chemokine-mediated disease states such as malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis, undesired hematopoeitic stem-cell release and diseases caused by respiratory, herpes and hepatitis viruses in which the chemokine binds to an interleukin (IL)-8 alpha or beta receptor by administering IL-8 receptor antagonists (I) or (II).

DETAILED DESCRIPTION - Chemokine-mediated disease states including malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis, undesired hematopoeitic stem-cell release and diseases caused by respiratory viruses, herpesviruses and hepatitis viruses in which the chemokine binds to an IL-8 alpha or beta receptor are treated by administering phenylurea compounds of formula (I) or (II) and their salts.

X = O or S;

R = any functional group with an ionizable hydrogen and a pKa of 10 or less;

R1 = H, halo, nitro, cyano, optionally halo-substituted 1-10C alkyl, 2-10C alkenyl, optionally halo-substituted 1-10C alkoxy, azide, (CR8R8)qS(O)tR4, hydroxy, 1-4C hydroxyalkyl, aryl, aryl-(1-4C) alkyl, aryloxy, aryl-(1-4C) alkyloxy, heteroaryl, heteroarylalkyl, heterocycle, heterocycle-(1-4C) alkyl, heteroaryl-(1-4C) alkyloxy, aryl-(2-10C) alkenyl, heteroaryl-(2-10C) alkenyl, heterocycle-(2-10C) alkenyl, (CR8R8)qNR4R5, 2-10C alkenyl-C(O)NR4R5, (CR8R8)qC(O)NR4R5, (CR8R8)qC(O)NR4R10, S(O)3H, S(O)3R8, (CR8R8)qC(O)R11, 2-10C alkenyl-C(O)R11, 2-10C alkenyl-C(O)OR11(CR8R8)qC(O)OR12, (CR8R8)qOC(O)R11, (CR8R8)qNR4C(O)R11, (CR8R8)qNHS(O)2R17, (CR8R8)qS(O)2NR4R5 or, two R1 together form O(CH2)sO or a 5-6-membered unsaturated ring;

q = 0-10;

m, s = 1-3;

t = 0-2;

v = 0-4;

R4, R5 = H, optionally substituted 1-4C alkyl, aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle or heterocycle-(1-4C) alkyl; or

R4 + R5 = form a 5-7-membered ring (optionally comprising an additional O, N or S);

HET = optionally substituted heteroaryl;

R8, R13, R14 = H or 1-4C alkyl;

R10 = 1-10C alkyl-C(O)2R8;

R11 = H, 1-4C alkyl or optionally substituted aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle, or heterocycle-(1-4C) alkyl;

R12 = H, 1-10C alkyl or optionally substituted aryl or arylalkyl;

R17 = 1-4C alkyl, aryl, arylalkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle or heterocycle-(1-4C) alkyl (all rings being optionally

substituted);
E = a group of formula (i)-(v); and
asterisk = point of attachment of the ring.
ACTIVITY - Protozoacide; vasotropic; antiarteriosclerotic; osteopathic; antiinflammatory; **virucide**; hepatotropic; antipsoriatic; dermatological; antiasthmatic; respiratory; antiulcer; cerebroprotective; thrombolytic; immunosuppressive; nephrotropic; nootropic; neuroprotective.
MECHANISM OF ACTION - IL-8 alpha receptor antagonist; IL-8 beta receptor antagonist. Compounds (I) had an IC50 of 1-30 micro g/ml in the permissive models for IL-8 receptor inhibition.
USE - (I) and (II) are used to treat chemokine-mediated diseases such as malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis, undesired hematopoeitic stem-cell release and diseases caused by respiratory viruses, herpesviruses and hepatitis viruses (claimed). They may be used to treat IL-8, GRO alpha , **GRO beta** , GRO gamma , NAP-2 and ENA-78-mediated diseases. They may be used to treat psoriasis, atopic dermatitis, arthritis, asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, inflammatory bowel disease, Crohn's disease, ulcerative colitis, stroke, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, cardiac and renal reperfusion injury, glomerulonephritis, thrombosis, graft-versus-host disease, Alzheimer's disease, allograft rejections, malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis, undesired hematopoeitic stem-cell release and diseases caused by respiratory viruses (rhinovirus, influenza virus), herpesviruses (herpes simplex I and II) and hepatitis viruses (hepatitis B and hepatitis C viruses).
Dwg.0/0

L78 ANSWER 26 OF 31 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-070950 [08] WPIDS
DOC. NO. CPI: C2001-019796
TITLE: New 2-phenylamino-3-phenyl quinazoline derivatives are interleukin-8 receptor antagonists used to treat e.g. psoriasis, atopic dermatitis, arthritis, asthma, inflammatory bowel disease and stroke.
DERWENT CLASS: B02
INVENTOR(S): PALOVICH, M R; WIDDOWSON, K L
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000073282	A1	20001207	(200108)*	EN	33

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AU BA BB BG BR CA CN CZ DZ EE GE GH GM HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ PL RO SG SI SK SL TR TT TZ UA US UZ VN YU ZA

AU 2000051689	A	20001218	(200118)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000073282	A1	WO 2000-US14659	20000526
AU 2000051689	A	AU 2000-51689	20000526

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000051689 A	Based on	WO 200073282

PRIORITY APPLN. INFO: US 1999-136667 19990528

AB WO 200073282 A UPAB: 20010207

NOVELTY - New 2-phenylamino-3-phenyl quinazoline derivatives (I) are new.

DETAILED DESCRIPTION - 2-Phenylamino-3-phenyl quinazoline derivatives of formula (I) and their salts are new.

R = OH, SH or NHSO2Rd;

Rd = NR6R7 or alkyl, aryl-(1-4C) alkyl, aryl-(2-4C) alkenyl, heterocyclyl or heterocyclyl-(1-4C) alkyl (all optionally substituted);

R6, R7 = H or 1-4C alkyl or

NR6R7 = optionally substituted 5-7-membered ring optionally containing an O, N or S heteroatom;

R1, Y = H, halo, nitro, cyano, 1-10C alkyl or 1-10C alkoxy (both optionally substituted by halo) , 2-10C alkenyl, azide, (CR8R8)qS(O)tR4, hydroxy, hydroxy-(1-4C) alkyl, aryl, aryl-(1-4C) alkyl, aryloxy, aryl-(1-4C) alkoxy, heteroaryl, heteroarylalkyl, heterocyclyl, heterocyclyl-(1-4C) alkyl, heteroaryl-(1-4C) alkoxy, aryl-(2-10C) alkenyl, heteroaryl-(2-10C alkenyl), heterocyclyl-(2-10C) alkynyl, (CR8R8)qNR4R5, 2-10C alkenyl-C(O)NR4R5, (CR8R8)qC(O)NR4R5, (CR8R8)qC(O)NR4R10, S(O)3H, S(O)3R8, (CR8R8)qC(O)R11, 2-10C alkenyl-C(O)R11, 2-10C alkenyl, C(O)OR11(CR8R8)qC(O)OR12, (CR8R8)qOC(O)R11, (CR8R8)qNR4C(O)R11, (CR8R8)qNHS(O)2R17 or (CR8R8)qS(O)2NR4R5, or

two R1 groups = O-(CH2)sO or a 5-6-membered unsaturated ring;

R2 = C(O), S(O), S(O)2 or C(NH);

q = 0-10;

t = 0-2;

s, m, n = 1-3;

R4, R5 = H, optionally substituted 1-4C alkyl, aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocyclyl, heterocyclyl-(1-4C) alkyl, or

NR4R5 = 5-7 membered ring optionally comprising an additional O, N or S heteroatom;

R8, R9 = H or 1-4C alkyl;

R10 = 1-10C alkyl C(O)2R8;

R11 = H, 1-4C alkyl, optionally substituted aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocyclyl or heterocyclyl-(1-4C) alkyl;

R12 = H, 1-10C alkyl or optionally substituted aryl or arylalkyl;

R17 = 1-4C alkyl or aryl, arylalkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocyclyl or heterocyclyl-(1-4C) alkyl (all optionally ring substituted) and

Ra = alkyl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocyclyl or heterocyclyl-(1-4C) alkyl (all optionally substituted).

ACTIVITY - Antipsoriatic; dermatological; antiinflammatory; antiarthritic; antiasthmatic; respiratory; gastrointestinal; cardiant; cerebroprotective; **antibacterial**; immunosuppressive; vasotropic; nephrotropic; thrombolytic; nootropic; neuroprotective; protozoacide; antiarteriosclerotic; osteopathic.

MECHANISM OF ACTION - Chemokine antagonist; interleukin-8 alpha receptor antagonist; interleukin-8 beta receptor antagonist; GRO receptor antagonist; neutrophil attractant/activation protein-2 receptor antagonist; ENA-78 receptor antagonist.

The interleukin-8 (IL-8) inhibitory effects of (I) were examined in vitro using Chinese hamster ovary cells in which high levels of recombinant human IL-8 type alpha and beta receptors were individually expressed by known methods (Holmes et al. Science 1991; 253: 1278).

Results showed that (I) exhibited IC50 values of 45 to less than 1 mu

g/ml in the permissive models for IL-8 receptor inhibition.
USE - Used to treat chemokine-mediated disease states such as psoriasis, atopic dermatitis, arthritis, asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, inflammatory bowel disease, Crohn's disease, ulcerative colitis, stroke, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, cardiac and renal reperfusion injury, glomerulonephritis, thrombosis, graft-versus-host reaction, Alzheimer's disease, allograft rejection, malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis and undesired hematopoeitic stem cell release. (I) Are also used to treat diseases mediated by GRO alpha , **GRO beta** , GRO gamma , neutrophils attractant/activation protein (NAP)-2 and ENA-78, primarily those characterized by massive neutrophil infiltration, T-cell infiltration or neovascular growth, and central nervous system injuries including open or penetrating head trauma caused by e.g. surgery, or closed head trauma injury, such as caused by an injury to the head region and including ischemic stroke, particularly to the brain area.
Dwg.0/0

L78 ANSWER 27 OF 31 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-070917 [08] WPIDS
DOC. NO. CPI: C2001-019763
TITLE: New phenylimino nitrogen containing heterocyclic compounds are chemokine inhibitors used for treating e.g. mediated disease in mammals.
DERWENT CLASS: B02 B03
INVENTOR(S): PALOVICH, M R; WIDDOWSON, K L
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000072845	A1	20001207	(200108)*	EN	39

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AU BA BB BG BR CA CN CZ DZ EE GE GH GM HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX MZ NO NZ PL RO SG SI SK SL TR TT TZ UA US UZ VN YU ZA

AU 2000051691 A 20001218 (200118)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000072845	A1	WO 2000-US14661	20000526
AU 2000051691	A	AU 2000-51691	20000526

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000051691	A	Based on	WO 200072845

PRIORITY APPLN. INFO: US 1999-136717 19990528
AB WO 200072845 A UPAB: 20010207
NOVELTY - New phenylimino nitrogen containing heterocyclic compounds (I) are new.
DETAILED DESCRIPTION - New phenylimino nitrogen containing heterocyclic compounds of formula (I) are new.
R = OH, SH or NHSO2Rd;

Rd = NR6R7, alkyl or aryl-1-4C alkyl, aryl-2-4C alkenyl, heteroaryl, heteroaryl-1-4C alkyl, heteroaryl-2-4C alkenyl, heterocyclyl, heterocyclyl-1-4C alkyl (all optionally ring substituted);

R6, R7 = H or 1-4C alkyl, or

NR6R7 = 5-7 membered ring optionally containing additional heteroatoms comprising O, N or S (optionally ring substituted);

R1 = H, halo, NO2, CN, 1-10C haloalkyl, 1-10C alkyl, 2-10C alkenyl, 1-10C alkoxy, 1-10C haloalkoxy, azide, (CR8R8)qS(O)tR4, OH, 1-4C hydroxyalkyl, aryl, aryl-1-4C alkyl, aryloxy, aryl-1-4C alkoxy, heteroaryl, heteroaralkyl, heterocyclyl, heterocyclyl-1-4C alkyl, heteroaryl 1-4C alkoxy, aryl-2-10C alkenyl, heteroaryl-2-10C alkenyl, heterocyclyl-2-10C alkenyl, (R8R8)qNR4R5, 2-10C alkenyl, C(O)NR4R5, (CR8R8)qC(O)NR4R5, (CR8R8)qC(O)NR4R10, SO3, SO3R8, (CR8R8)qC(O)R11, 2-10C alkenyl C(O)R11, 2-10C alkenyl CO2R11(CR8R8)qCO2R12, (CR8R8)qOC(O)R11, (CR8R8)qNR4C(O)R11, (CR8R8)qNHSO2R17 or (CR8R8)qSO2NR4R5, or

R1 + R1 = O(CH2)sO or 5-6 membered unsaturated ring;

R2 = 2-5C alkyl or 2-5C alkenyl (both optionally substituted by 1-3 halo, NO2, 1-4C haloalkyl, 1-4C alkyl, amino, mono- or di-(1-4C alkyl) amine, OH, 1-4C alkoxy, NR9C(O)Ra, S(O)mRa, C(O)NR6R7, CO2H, CO2Ra, SO2NR6R7, NHSO2Ra and optionally containing 1-3 NR9, O, S(O), S, SO or SO2);

R3 = 1-10C alkyl, 1-10C haloalkyl, 2-10C alkenyl, 1-10C alkoxy, 1-10C haloalkoxy, azide, SOtR4, (CR8R8)qSOtR4, OH, 1-4C hydroxyalkyl, aryl, aryl-1-4C alkyl, aryl-2-10C alkenyl, aryloxy, aryl-1-4C alkoxy, heteroaryl, heteroaralkyl, heteroaryl-2-10C alkenyl, heteroaryl-1-4C alkoxy, heterocyclyl, heterocyclyl-1-4C alkyl, heterocyclyl-1-4C alkoxy, heterocyclyl-2-10C alkenyl, (CR8R8)qNR4R5, (CR8R8)qC(O)NR4R5, 2-10C alkenyl C(O)NR4R5, (CR8R8)qC(O)NR4R10, SO3R8, (CR8R8)qC(O)R11, (CR8R8)qNR4C(O)R11, (CR8R8)qC(NR4)NR4R5, (CR8R8)qOC(O)R11, (CR8R8)qNR4C(O)R11, (CR8R8)qC(NR4)NR4R5, (CR8R8)qNR4C(NR5)R11, (CR8R8)qNHSO2R13 or (CR8R8)qSO2NR4R5 (all optionally alkyl or ring substituted), or

R3 + R3 = O(CH2)sO or 5-6 membered optionally unsaturated ring (both optionally alkyl or ring substituted);

q = 0-10;

t = 0-2;

s = 1-3;

R4, R5 = H or 1-4C alkyl, aryl, aryl-1-4C alkyl, heteroaryl or heteroaryl-1-4C alkyl (all optionally substituted), heterocyclyl or heterocyclyl-1-4C alkyl, or

NR4R5 = 5-7 membered ring (optionally containing an additional heteroatom comprising O, N or S);

Y = H, halo, NO2, CN, 1-10C haloalkyl, 1-10C alkyl, 2-10C alkenyl, 1-10C alkoxy, 1-10C haloalkoxy, azido, (CR8R8)qSOtR4, OH, 1-4C hydroxyalkyl, aryl, aryl-1-4C alkyl, aryloxy, aryl-1-4C alkoxy, heteroaryl, heteroaralkyl, heteroaryl-1-4C alkoxy, heterocyclyl, heterocyclyl-1-4C alkyl, aryl-2-10C alkenyl, heteroaryl-2-10C alkenyl, heterocyclyl-2-10C alkenyl, (CR8R8)qNR4R5, 2-10C alkenyl, C(O)NR4R5, (CR8R8)2C(O)NR4R5, (CR8R8)qC(O)NR4R10, SO3H, SO3R8, (CR8R8)qC(O)R11, 2-10C alkenylC(O)R11, 2-10C alkenylCO2R11, C(O)R11, (CR8R8)qC(O)R11, 2-10C alkenylC(O)R11, 2-10C alkenylCO2R11, C(O)R11, (CR8R8)qCO2R12, (CR8R8)qOCOR11, (R8R8)qNR4C(O)R11, (CR8R8)qNHSO2Rd or (CR8R8)qSO2NR4R5 or

Y + Y = O(CH2)sO or 5-6 membered unsaturated ring;

n, m = 1-3;

R8, R9 = H or 1-4C alkyl;

R10 = 1-10C alkylCO2R8;

R11 = H, 1-4C alkyl or aryl, aryl-1-4C alkyl, heteroaryl, heteroaryl-1-4C alkyl, heterocyclyl or heterocyclyl-1-4C alkyl (all optionally substituted);

R12 = H, 1-10C alkyl or aryl or aralkyl (both optionally substituted);

R17 = 1-4C alkyl, aryl, aralkyl, heteroaryl, heteroaryl-1-4C alkyl, heterocyclyl or heterocyclyl-1-4C alkyl (all optionally ring substituted) and

Ra = alkyl, aryl, aryl-1-4C alkyl, heteroaryl, heteroaryl-1-4C alkyl, heterocyclyl or heterocyclyl-1-4C alkyl (all optionally substituted).

ACTIVITY - Antipsoriatic; dermatological; antiarthritic; antiasthmatic; respiratory; gastrointestinal; cerebroprotective; **antibacterial**; immunosuppressive; cardiant; vasotropic; nephrotropic; thrombolytic; neuroprotective; protozoacide; antiarteriosclerotic; osteopathic.

MECHANISM OF ACTION - Chemokine antagonist; interleukin-8 (IL-8) alpha receptor antagonist; IL-8 beta receptor antagonist; GRO alpha antagonist; **GRO beta** antagonist; GRO gamma antagonist; neutrophil attractant/activation protein-2 antagonist; ENA-78 antagonist.

In a receptor binding assay using (125)IL-8 (human recombinant), (I) e.g. 4-((3-(2-bromophenyl)-4-oxo-1-(phenylmethyl)-2-imidazolidinylidene)imino)-3-hydroxybenzonitrile (Ia) exhibited IC50 values of 45 to less than 1 mu g/ml.

USE - Used for treating psoriasis, atopic dermatitis, arthritis, asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, inflammatory bowel disease, Crohn's disease, ulcerative colitis, stroke, septic shock, endotoxic shock, gram negative sepsis, toxic shock syndrome, cardiac and renal reperfusion injury, glomerulonephritis, thrombosis, graft versus host reaction, Alzheimer's disease, allograft rejections, malaria, restenosis, angiogenesis, atherosclerosis, osteoporosis, gingivitis and undesired hematopoietic stem cell release.

Dwg.0/0

L78 ANSWER 28 OF 31 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-339300 [29] WPIDS
DOC. NO. CPI: C2000-102881
TITLE: New cyclic pyridyl substituted compounds, useful for treating chemokine-mediated diseases such as psoriasis, atopic dermatitis and asthma.
DERWENT CLASS: B02
INVENTOR(S): WIDDOWSON, K L
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000021963	A1	20000420	(200029)*	EN	51

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000021963	A1	WO 1999-US23776	19991012

PRIORITY APPLN. INFO: US 1998-104016 19981013
AB WO 200021963 A UPAB: 20000617
NOVELTY - Cyclic pyridyl substituted compounds (I) and their salts are new.

DETAILED DESCRIPTION - Cyclic pyridyl substituted compounds of formula (I) are new.

R = NHC(X)NH(CR13R14)v-Z;

R1 = H, halo, nitro, cyano, halo-substituted 1-10C alkyl,

(CR8R8)qS(O)tR4, hydroxy, hydroxy-(1-4C) alkyl, aryl, aryl-(1-4C) alkyl, aryloxy, aryl-(1-4C) alkyloxy, heteroaryl, heteroarylalkyl, heterocycle, heterocycle-(1-4C) alkyl, heteroaryl-(1-4C) alkyloxy, aryl-(2-10C) alkenyl, heteroaryl-(2-10C) alkenyl, heterocycle-(2-10C) alkenyl, (CR8R8)qNR4R5, 2-10C alkenyl-C(O)NR4R5, (CR8R8)qC(O)NR4R5, (CR8R8)qC(O)NR4R10, S(O)3R8, (CR8R8)qC(O)R11, 2-10C alkenyl-C(O)R11, 2-10C alkenyl-C(O)OR11, C(O)R11, (CR8R8)qC(O)OR12, 2-10C alkenyl-OC(O)R11, (CR8R8)qNR4C(O)R11, (CR8R8)qNR4C(O)R11, (CR8R8)qC(NR4)NR4R5, (CR8R8)qNR4C(NR5)R11, (CR8R8)qNHS(O)2R17 or (CR8R8)qS(O)2NR4R5 (all aryl, heteroaryl and heterocyclic groups are optionally substituted);

m = 1-3;

X = O or S;

Z = W, Het, a group of formula (i) or optionally substituted 1-10C alkyl, 2-10C alkenyl or 2-10C alkynyl;

n, p, s = 1-3;

q = 0-10;

t = 0-2;

v = 0-4;

Het = heteroaryl;

R4, R5 = H, optionally substituted 1-4C alkyl, aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle or heterocycle-(1-4C) alkyl (all optionally substituted) or, together with the N to which they are attached, form a 5-7-membered ring optionally comprising an additional heteroatom chosen from O, S or N;

Y = H, halo, nitro, cyano, halo-substituted 1-10C alkyl, (CR8R8)qS(O)tR4, hydroxy, hydroxy-(1-4C) alkyl, aryl, aryl-(1-4C) alkyl, aryloxy, aryl-(1-4C) alkyloxy, heteroaryl, heteroarylalkyl, heteroaryl-(1-4C) alkyloxy, heterocycle, heterocycle-(1-4C) alkyl, aryl-(2-10C) alkenyl, heteroaryl-(2-10C) alkenyl, heterocycle-(2-10C) alkenyl, (CR8R8)qNR4R5, 2-10C alkenyl-C(O)NR4R5, (CR8R8)qC(O)NR4R5, (CR8R8)qC(O)NR4R10, S(O)3R8, (CR8R8)qC(O)R11, 2-10C alkenyl-C(O)R11, 2-10C alkenyl-C(O)OR11, (CR8R8)qC(O)OR12, (CR8R8)qNR4C(O)R11, (CR8R8)qNR4C(O)R11, (CR8R8)qC(NR4)NR4R5, (CR8R8)qNR4C(NR5)R11, (CR8R8)qNHS(O)2Ra or (CR8R8)qS(O)2NR4R5 (all aryl, heteroaryl and heterocyclic groups are optionally substituted); or

two Y groups together may form O-(CH2)sO or a 5-6-membered optionally saturated ring;

R8 = H or 1-4C alkyl;

R10 = 1-10C alkyl-C(O)2R8;

R11 = H, 1-4C alkyl or aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle or heterocycle-(1-4C) alkyl (all optionally substituted);

R12 = H, 1-10C alkyl or optionally substituted aryl or arylalkyl;

R13, R14 = H, optionally substituted 1-4C alkyl or one is optionally substituted aryl;

R17 = 1-4C alkyl or aryl, aryl-(1-4C) alkyl, heteroaryl, heteroaryl-(1-4C) alkyl, heterocycle or heterocycle-(1-4C) alkyl (all optionally substituted);

R18 = H, optionally substituted 1-10C alkyl, optionally halo-substituted 1-10C alkoxy, hydroxy, aryl-(1-4C) alkyl, aryl-(2-4C) alkenyl, heteroaryl, heteroaryl-(2-4C) alkyl, heterocycle or heterocycle-(1-4C) alkyl (all aryl, heteroaryl and heterocycle groups optionally substituted);

Ra = NR4R5, alkyl, aryl-(1-4C) alkyl, aryl-(2-4C) alkenyl, heteroaryl, heteroaryl-(1-4C) alkyl, heteroaryl-(2-4C) alkenyl, heterocycle or heterocycle-(1-4C) alkyl (all aryl, heteroaryl and heterocycle groups optionally substituted);

W = group of formula (ii) or (iii);

E-containing ring = a group of formula (iv)-(vii);

asterisk = attachment point.

N.B. R15 and R16 are not defined in the claims. In the disclosure,

R15, R16 = H or an optionally substituted 1-4C alkyl. R18 is defined but does not appear in the formulae or definitions.

INDEPENDENT CLAIMS are also included for:

(1) intermediates of formula (II);

(2) methods of preparation of (I) and (II).

ACTIVITY - Dermatological; antiasthmatic; antiarthritic; antiinflammatory; antiulcer; antibacterial; immunosuppressive; cerebroprotective; nephrotic; thrombolytic; nootropic; neuroprotective.

MECHANISM OF ACTION - Interleukin (IL)-8 receptor antagonist; GRO alpha receptor antagonist, GRO beta receptor antagonist, GRO gamma receptor antagonist, neutrophils attractant protein (NAP)-2 receptor antagonist; ENA-78 receptor antagonist.

USE - (I) are used to treat IL-8-, GRO alpha -, GRO beta -, GRO gamma -, NAP-2- and ENA-78-mediated diseases. They are used to treat chemokine-mediated diseases in mammals including psoriasis, atopic dermatitis, asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, arthritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, stroke, cardiac and renal reperfusion injury, glomerulonephritis, thrombosis, Alzheimer's disease, graft-versus-host reaction or allograft rejection (claimed) as well as malaria, restenosis, angiogenesis or undesired hematopoietic stem-cell release, rhinovirus infection and bone resorption indications.

Dwg.0/0

L78 ANSWER 29 OF 31 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-317441 [27] WPIDS
DOC. NO. CPI: C2000-095969
TITLE: Use of new or known neoangiogenesis marker-active agent conjugates for tumor diagnosis and/or therapy, are targeted to the required sites with high specificity.
DERWENT CLASS: B04 K08
INVENTOR(S): KRAUSE, W; MUSCHICK, P
PATENT ASSIGNEE(S): (SCHD) SCHERING AG
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000018439	A2	20000406	(200027)*	GE	27
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AE AL AM AU AZ BA BB BG BR BY CA CN CR CU CZ DM EE ES GD GE GH GM HR HU ID IL IN IS JP KG KP KR KZ LC LK LR LS LT LV MD MG MK MN MW MX NO NZ PL PT RO RU SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
DE 19845798	A1	20000413	(200027)		
AU 2000012642	A	20000417	(200035)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000018439	A2	WO 1999-EP7198	19990929
DE 19845798	A1	DE 1998-19845798	19980929
AU 2000012642	A	AU 2000-12642	19990929

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000012642	A Based on	WO 200018439

PRIORITY APPLN. INFO: DE 1998-19845798 19980929
AB WO 200018439 A UPAB: 20000606
NOVELTY - The use of neoangiogenesis marker (NAGM)-active agent conjugates (I)-(IV) as agents for the diagnosis and/or therapy of tumors is new. Some of the conjugates, containing specific active agents, are new compounds.

DETAILED DESCRIPTION - The use of neoangiogenesis marker (NAGM)-active agent conjugates of formula (I)-(IV) is claimed as agents for the diagnosis and/or therapy of tumors.

N = NAGM residue derived from NAGM's, NAGM partial sequences, NAGM receptor agonists or antagonists or antibodies or antibody fragments;

L1, L2 = direct bond or bridging group;

Z = central unit, e.g. a C, N, P, O or S atom or an alkyl or aryl group (optionally substituted or interrupted by heteroatoms);

P1, P2 = polymer residues linked via suitable functional groups;

W1 = active group comprising (i) a diagnostic agent selected from magnetic resonance imaging, X-ray, ultrasonic and near-infrared contrast agents or (ii) a therapeutic agent selected from radiosensitizers, photosensitizers, chemotherapeutic agents, PTK blockers, growth factor inhibitors, antiproliferative agents, antibodies, antibody fragments, peptides, carbohydrates and oligonucleotides;

W2 = active group selected from (i) as for W1 (i), (ii), radionuclides of the elements Ag, As, At, Au, Ba, Bi, Br, C, Co, Cr, Cu, F, Fe, Ga, Gd, Hg, Ho, I, In, Ir, Lu, Mn, N, O, P, Pb, Pd, Pt, Pm, Re, Rh, Ru, Sb, Sc, Se, Sm, Sn, Tb, Tc and Y or (iii) a radiosensitizer, photosensitizer or drug (specifically a chemotherapeutic agent, cytostatic agent, PTK blocker, growth factor inhibitor or antiproliferative agent);

R, Q = bridging groups such that the bond can be cleaved in the body; preferably R-Q is a disulfide, amide, ester, anhydride, thioamide, thioanhydride or urea group;

m, n, o, p = preferably (sic) 1-100.

INDEPENDENT CLAIMS are also included for:

(a) the preparation of (I)-(IV), by coupling NAGM with a diagnostic or therapeutic agent, coupling NAGM with an active agent via a bridging member or coupling one or more NAGM and one or more active agent(s) onto the same carrier molecule; and

(b) (I)-(IV) as new compounds, provided that:

W1 or W2 = (i) vinblastine, doxorubicin, bleomycin, methotrexate, 5-fluorouracil, 6-thioguanine, cytarabine, cyclophosphamide or cisplatin residue; (ii) quercetin, genistein, erbstatin, lavendustin A, herbimycin A, aeoplysinin-1-tyrphostine, S-aryl-benzylidene-malononitrile or benzylidene malononitrile residue; (iii) mercaptopurine, N-methylformamide, 2-amino-1,3,4-thiadiazole, melphalan, hexamethyl-melamine, gallium nitrate, 3% thymidine, dichloromethotrexate, mitoguazone, sumarin, bromodeoxyuridine, semustine, 1-(2-chloroethyl)-3-(2,6-dioxo-3-piperidinyl)-1-nitrosourea, N,N'-hexamethylene-bis-acetamide, azacitidine, dibromodulcitol, Erwinia asparaginase, ifosfamide, 2-mercaptoethanesulfonate, teniposide, taxol, 3-deazauridine, folic acid antagonist, homoharringtonine, cyclo-cytidine, acivicin, ICRF-187, spiromustine, levamisole, chlorozotocin, aziridinyl-benzoquinone, spirogermanium, aclarubicin, pentostatin, PALA, carboplatin, amsacrine, caracemide, iproplatin, misonidazole, dihydro-5-azacytidine, 4'-deoxy-doxorubicin, menogaril, triciribin phosphate, fazarabine, tiazofurin, teroxirone, ethiofos, N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide, mitoxantrone, acodazole, amonafid, fludarabine phosphate, pibenzimol, didemnin B, merbarone, dihydrolenperone, flavone-8-acetic acid, oxantrole, ipomeanol, trimetrexate, deoxyspergualin, echinomycin or dideoxy-cytidine residue; (iv) a derivative of anti-PDGF or a triazolopyrimidine; (v) colchicine, angiopeptin, extradiol or an ACE-inhibitor; or (vi) simvastatin or probucol.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - PTK blocker; growth factor inhibitor.
USE - For the diagnosis or therapy of tumors.
Typically implanted VX2 tumors in rabbits were detected by intravenously injecting a solution of rhenium-186-labeled N-(N', N', N''',N'''-tetrakis-(hydroxy-carboxy-methyl)-N''-(carboxymethyl)-diethylene triamino)-Thy-1-antibody (activity 10 MBq; volume 1 ml) and obtaining scintigrams after 2, 4, 6, 8, 12 and 24 hours using a conventional gamma -camera; tumors were identified by elevated radiation intensity.
ADVANTAGE - Coupling with NAGM gives the active agent high specificity, so that levels are enriched at the target site (even on use at low doses) for a sufficent time to provide the required effect. Toxic concentrations are not reached in other tissues, conjugates not bonded to target receptor sites are rapidly eliminated from the body and systemic side-effcts are minimized. Some of the conjugates are more readily taken up by the cells at the target site, as well as being effectively transported to the diseased location.
Dwg.0/0

L78 ANSWER 30 OF 31 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-195265 [17] WPIDS
DOC. NO. NON-CPI: N2000-144448
DOC. NO. CPI: C2000-060555
TITLE: New multifunctional compounds useful for preventing and/or treating malignant cell growth and for detection and diagnosis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BAEUERLE, P A; BORSCHERT, K; DREIER, T; KUFER, P; ZETTL, F
PATENT ASSIGNEE(S): (MICR-N) MICROMET GES BIOMEDIZINISCHE FORSCHUNG
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000006605	A2	20000210	(200017)*	EN	165

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

AU 9957289	A	20000221	(200029)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000006605	A2	WO 1999-EP5416	19990728
AU 9957289	A	AU 1999-57289	19990728

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9957289	A	Based on	WO 200006605

PRIORITY APPLN. INFO: EP 1998-114082 19980728
AB WO 200006605 A UPAB: 20000405
NOVELTY - New multifunctional compounds comprise a heavy chain constant domain and a light chain constant domain with at least two fused polypeptides having different receptor or ligand functions.

DETAILED DESCRIPTION - A multifunctional compound (A) produceable in a mammalian host cell as a secretable and fully functional heterodimer of two polypeptide chains, where one of the polypeptide chains comprises, as the only constant region domain of an immunoglobulin heavy chain the CH1-domain and the other polypeptide chain comprises the constant CL-domain of an immunoglobulin light chain, where the polypeptide chains further comprise, fused to the constant region domains at least two (poly)peptides having different receptor or ligand functions, where further at least two of the different (poly)peptides lack an intrinsic affinity for one another and where the polypeptide chains are linked via the constant domains.

INDEPENDENT CLAIMS are also included for the following:

(1) a polynucleotide (PN) encoding one and/or two polypeptide chains of the multifunctional compound as in (A);

(2) a vector comprising at least one PN as in (1);

(3) a mammalian host cell comprising at least one vector as in (2);

(4) a method of producing (A) comprising culturing the host cell of (3) and recovering (A) from the culture; and

(5) a kit comprising a multifunctional compound as in (A) and, optionally, a proteinaceous compound capable of providing the primary activation signal for T-cells.

ACTIVITY - Cytostatic; immunostimulatory; antileukemia; antiproliferative.

A protein was constructed that connected the single-chain Fv fragment (scFv) of the murine anti 17-1A anti-gastric cancer cell antibody M79 with the extracellular domains of human CD80 by virtue of the heterodimeric association of the immunoglobulin domains CH1 from the human gamma 1 heavy chain and Ckappa, the constant region of the human kappa light chain. For this purpose the M79scFv was connected to the human CH1 and the extracellular part of human CD80 was joined to human Ckappa, the resulting polypeptide encoding chains were inserted into separate expression vectors and both transfected into the same mammalian host cell line resulting in the CD80 heterominibody . The CD80 heterominibody produced was shown to bind immobilized 17-1A antigen. Heterominobodies containing 3 further costimulatory (CD86) or adhesion proteins (CD54, CD58) were constructed. CD54, CD58 and CD86 were introduced into the heterominibodies by PCR cloning. The heterominibodies were shown to be able to stimulate T-cells.

MECHANISM OF ACTION - None given.

USE - The multifunctional compounds can be used for preventing and/or treating malignant cell growth, e.g. lymphomas, leukemias, carcinomas, melanomas, or sarcomas. The compounds can also be used for detection and diagnosis.

ADVANTAGE - The CL and CH1 (solely by themselves) can provide sufficient dimerization forces capable of joining different receptors or ligands which normally do not associate. The products allow heterodimerization of 2 different (poly)peptide chains without any intrinsic affinity to each other in a single host expression system.

Dwg.0/61

L78 ANSWER 31 OF 31 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-100344 [09] WPIDS
CROSS REFERENCE: 1993-167397 [20]; 1995-131186 [17]; 1997-033572 [03]
DOC. NO. NON-CPI: N1998-080433
DOC. NO. CPI: C1998-033079
TITLE: Antibody to CD8+ cell **antiviral** factor - used for the inhibition of retroviral replication, especially used to treat HIV infection.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): LEVY, J A; MACKEWICZ, C E
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5707814	A	19980113	(199809)*		8

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 5707814	A	CIP of	US 1991-786114	19911101
		CIP of	WO 1992-US9302	19921030
		CIP of	US 1993-122221	19930917
		CIP of	US 1994-307179	19940916
			US 1996-610942	19960305

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 5707814	A	CIP of	US 5565549
		CIP of	US 5580769

PRIORITY APPLN. INFO: US 1996-610942 19960305; US 1991-786114 19911101; WO 1992-US9302 19921030; US 1993-122221 19930917; US 1994-307179 19940916

AB US 5707814 A UPAB: 19980302

A new antibody which is immunospecific to a CD8+ cell **antiviral** factor (CAF) has the following characteristics: (a) blocks viral replication by inhibiting viral RNA transcription; (b) does not affect CD4+ cell activation or proliferation; (c) is not a cytokine selected from IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-16, **G-CSF**, GM-CSF, TNF alpha , TNF beta , IFN alpha , IFN beta , IFN gamma , TGF beta , RANTES, MIP-1 alpha , MIP-1 beta , MCP-1, MCP-3, IP-10, lymphotactin, GRO- alpha , **GRO-beta** and LIF; and (d) is not a soluble TNF alpha -I or TNF alpha -II receptor.

Also claimed is a method for inhibiting retroviral replication in cells, comprising exposing the cells to a substantially pure composition of CD8+ CAF which: (a) blocks viral replication by inhibiting viral RNA transcription; (b) does not affect CD4+ cell activation or proliferation; (c) is not a cytokine selected from IL-1, IL-2, IL-3, IL-4, IL- 5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-16, **G-CSF**, GM-CSF, TNF alpha , TNF beta , IFN alpha , IFN beta , IFN gamma , TGF beta , RANTES, MIP-1 alpha , MIP-1 beta , MCP-1, MCP-3, IP-10, lymphotactin, GRO- alpha , **GRO- beta** and LIF; (d) is not a soluble TNF alpha -I or TNF alpha -II receptor; (e) is released from activated CD8+ cells; (f) is inactivated at pH 10-12 but not at pH 2-8; (g) retains about 60% of its activity when heated at 100 deg. C for 30 min; (i) is resistant to trypsin; (j) is not inactivated by freeze-thawing; (k) is sensitive to staph V8 protease but not to protease type XIA (proteinase K); (l) does not induce 2'-5'-A synthetase in CD4+ lymphocytes; (m) is precipitated from CD8+ cell supernatant by 53% ammonium sulphate; (n) is lipid-free; and (o) contains none of the cytokines of (c) nor the soluble receptors of (d).

USE - The antibody is useful for monitoring the effectiveness of treatment of HIV infections by determining the effect of an administered drug on CAF levels (preferably by ELISA) or the number of CD8+ lymphocytes expressing CAF on their surface (preferably by flow cytometry); and for detecting CAF on the surface of CD8+ cells by flow cytometry.

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